CLAIMS

1. A method to evaluate the presence of high levels of autoantibodies against endothelial PC / activated PC receptor (EPCR) in a sample, characterised by comprising the *in vitro* quantification of autoantibodies against EPCR in said sample from a subject.

2. Method according to claim 1, characterised by said presence of high levels of autoantibodies against EPCR being related to a pathology selected from autoimmune disease, vascular disease and obstetric complications.

3. Method according to any of claims 1 or 2, characterised in that said autoimmune disease is selected from antiphospholipid syndrome, systemic lupus erythematosus, rheumatoid arthritis and autoimmune vasculitis.

4. Method according to any of claims 1 or 2, characterised in that said vascular disease is selected from arterial vascular disease, venous vascular disease and thrombosis of the microcirculation.

5. Method according to claim 4, characterized in that said vascular disease is selected from myocardial infarction, cerebral stroke, a transient cerebrovascular accident, limb ischemia, atherosclerosis, aneurysm, thrombosis, superficial venous thrombosis, deep venous thrombosis, and pulmonary embolism.

6. Method according to any of claims 1 or 2, characterized in that said obstetric complication is selected from miscarriage, fetal death, premature birth, delayed intrauterine growth, eclampsia and pre-eclampsia.

7. Method according to any of claims 1 to 6, characterized in that the mentioned sample is a sample of serum or plasma.

8. Method according to any of claims 1 to 7, characterized in that the mentioned subject is human.

9. Method according to any of claims 1 to 8, characterized in that quantification of these anti-EPCR autoantibodies is carried out by means of an immunoassay coupled to a marker.

10. Method according to any of claims 1 to 9, characterized in that quantification of these anti-EPCR autoantibodies is carried out by means of an ELISA test comprising:

a) solid support immobilization of a polypeptide comprising the EPCR amino acid sequence or a fragment thereof containing at least one epitope that can be recognized by an anti-EPCR autoantibody;
b) incubation of the immobilized polypeptide with a sample suspected to contain anti-EPCR autoantibodies, obtained from the subject, for sufficient time to allow binding of the antibodies to the immobilized polypeptide, and the formation of polypeptide-anti-EPCR autoantibody complexes;
c) removal of the remaining sample not bound to the immobilized polypeptide;
d) incubation of the polypeptide-anti-EPCR autoantibody complexes with a second antibody conjugated to an enzyme, where the second antibody is able to bind to these anti-EPCR autoantibodies.

11. Method according to claim 10, characterized in that the mentioned polypeptide is selected from between:

a) a polypeptide comprising the sequence of amino acids of full length EPCR; and

b) a polypeptide comprising the sequence of amino acids of a fragment of EPCR containing at least one epitope capable of being recognized by an anti-EPCR antibody.

12. Method according to any of claims 1 to 11, characterised in that said polypeptide is a fusion protein comprising:

a) a region A composed of a polypeptide containing the EPCR amino acid sequence or a fragment thereof containing at least one epitope capable of being recognized by an anti-EPCR antibody; and

b) a region B composed of a polypeptide comprising a sequence of amino acids of use for isolating or purifying the mentioned fusion protein, and/or a sequence of amino acids of use for anchoring the mentioned fusion protein to a solid support.

13. Method according to claim 12, characterized in that said region B is bound to the amino terminal extreme of region A.

14. Method according to claim 12, characterized in that said region B is bound to the carboxyl terminal extreme of region A.

15. Method according to any of claims 12 to 14, characterized in that said region A comprises the amino acid sequence of the soluble part of human EPCR.

16. Method according to any of claims 12 to 14, in which the amino acid sequence of use for isolating or purifying the

mentioned fusion protein, and/or an amino acid sequence of use for anchoring said fusion protein to a solid support present in region B, comprises a sequence of amino acids selected from Arg-tag, His-tag, FLAG-tag, Strep-tag, an epitope capable of being recognized by antibody, SBP-tag, S-tag, calmodulin binding peptide, cellulose binding domain, chitin binding domain, glutathione S-transferase-tag, maltose binding protein, NusA, TrxA, DsbA, Avi-tag, Ala-His-Gly-His-Arg-Pro (SEQ ID NO: 4) (2, 4, and 8 copies), Pro-Ile-His-Asp-His-Asp-His-Pro-His-Leu-Val-Ile-His-Ser (SEQ ID NO: 5), Gly-Met-Thr-Cys-X-X-Cys (SEQ ID NO: 6) (6 repetitions), β-galactosidase and VSV-glycoprotein.

17. Method according to any of claims 12 to 16, characterised in that region B is composed of a polypeptide comprising a c-myc epitope capable of being recognized by an anti-c-myc antibody and a tail of histidines (His-tag).

18. Method according to any of claims 12 to 17, characterised in that said polypeptide is a fusion protein comprising the sequence of amino acids of the soluble part of human EPCR, the sequence of amino acids corresponding to c-myc epitope and a tail of histidines (His-tag).

19. Method according to any of claims 12 to 18, characterised in that said polypeptide is a fusion protein whose sequence of amino acids is shown in SEQ ID NO: 3.

20. Method according to claim 10, characterised in that said second antibody is an immunoglobulin isotype-specific antibody originating from a species different to that of the subject whose sample is being tested.

21. Method according to claims 10 or 20, characterised in

that said second immunoglobulin isotype-specific antibody is selected from an anti-human IgG antibody, an anti-human IgM antibody, an anti-human IgA antibody, and their mixtures.

22. Method according to any of claims 20 or 21, characterised in that said second antibody is conjugated to an enzyme selected from between peroxidase and alkaline phosphatase.

23. Method according to any of claims 1 to 22, characterised in that it moreover comprises the comparison of anti-EPCR autoantibody levels determined in the sample from the subject versus normal levels.

24. A method according to claim 1, characterized in determining the variation in the levels of anti-EPCR autoantibodies over a given time period.

25. Method according to claim 24, characterized in that said sample originates from a subject previously diagnosed with an autoimmune or vascular disease, or who has suffered an obstetric complication, and is subject to therapeutic treatment.

26. Use of autoantibodies against EPCR in a method to evaluate the presence of high levels of autoantibodies against EPCR in a sample.

27. Use according to claim 26, characterised in that the mentioned presence of high levels of autoantibodies against EPCR in a sample is associated to a pathology selected from an autoimmune disease, a vascular disease and obstetric complications.

28. Use of a polypeptide comprising the EPCR amino acid sequence or a fragment thereof containing at least one epitope capable of being recognized by an anti-EPCR autoantibody in a method to the presence of high levels of autoantibodies against EPCR in a sample, characterised by comprising *in vitro* quantification of autoantibodies against EPCR in said sample.

29. Use according to claim 28, characterised in that said pathology related to the presence of high levels of autoantibodies against EPCR is selected from autoimmune disease, vascular disease and obstetric complications.

30. Use according to claim 28, characterised in that said polypeptide is a fusion protein comprising:

a) a region A composed of a polypeptide containing the EPCR amino acid sequence or a fragment thereof containing at least one epitope capable of being recognized by an anti-EPCR antibody; and

b) a region B composed of a polypeptide comprising a sequence of amino acids of use for isolating or purifying said fusion protein, and/or a sequence of amino acids of use for anchoring said fusion protein to a solid support.

31. Use of a polypeptide according to claim 30, in which said region A comprises the amino acid sequence of the soluble part of human EPCR.

32. Use according to any of claims 30 or 31, characterized in that said polypeptide is a fusion protein comprising the amino acid sequence of the soluble part of human EPCR, the sequence of amino acids corresponding to c-myc epitope and a tail of histidines (His-tag).

33. Use of a polypeptide according to any of claims 30 to 32, characterised in that said polypeptide is a fusion protein with the amino acid sequence shown in SEQ ID NO: 3.

34. A kit for *in vitro* evaluation of the presence of high levels of autoantibodies against EPCR in a sample, characterised in that said kit comprises a polypeptide that comprises the EPCR amino acid sequence or a fragment thereof containing at least one epitope capable of being recognized by an anti-EPCR autoantibody.

35. A kit according to claim 34, characterised in that said polypeptide is a fusion protein comprising:

i) a region A composed of a polypeptide containing the EPCR amino acid sequence or a fragment thereof containing at least one epitope capable of being recognized by an anti-EPCR antibody; and

ii) a region B composed of a polypeptide comprising an amino acid sequence of use for isolating or purifying the mentioned fusion protein, and/or an amino acid sequence of use for anchoring the mentioned fusion protein to a solid support.

36. A kit according to claim 35, in that said region A is characterized by comprising the amino acid sequence of the soluble part of human EPCR.

37. A kit according to any of claims 35 or 36, characterised in that said polypeptide is a fusion protein comprising the amino acid sequence of the soluble part of human EPCR, the amino acid sequence corresponding to c-myc epitope and a tail of histidines (His-tag).

38. A kit according to any of claims 35 to 37,

characterised in that said polypeptide is a fusion protein with the sequence of amino acids shown in SEQ ID NO: 3.